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### **REMARKS/ARGUMENTS**

In response to the Rejection mailed August 23, 2004, applicants have amended claims 53, 60 and 61, added new claims 62 and 63 and present the following remarks. Claims 1-51 and 54-56 have been canceled. Claims 52-53 and 57-63 are pending.

Claims 53, 60 and 61 were objected to as containing informalities. These claims have been amended accordingly.

Claim 53 was rejected under 35 USC 112, first paragraph, as having subject matter not adequately described in the specification. Specifically, the rejection alleges that the specification does not adequately describe the detection techniques, which can be used to detect a band of particles in the lower region wherein the detection technique cannot be used if the band is in the upper region. This rejection is traversed.

The specification at several locations mentioned detecting the band of particles by optical techniques such as detecting fluorescence, light scattering, etc. For example, see the Abstract or Summary of the Invention, first paragraph.

The specific dimensions given for the centrifuge tube provided in the sentence bridging pages 10 and 11 of the specification provides for approximately a 10,000 fold decrease in cross section area between the top and the lowest regions. It should not surprise anyone that one could easily detect a fluorescent band, which is 10,000 times more concentrated than a fluorescent band that is not detectable. One of ordinary skill would expect many other detection techniques useful for detecting something after 10,000 fold concentration.

The rejection also mentions on page 4 that "the skilled artisan cannot envision a detection technique recited in claim 53...until reduction to practice has occurred." This is a curious statement because as a factual matter, actual reduction to practice occurred long ago and has been used many times before the filing date of the present application. Details for one example were given in the EXAMPLE section of the specification. Accordingly, this rejection should be withdrawn.

Claims 52, 53 and 57-61 were rejected under 35 USC 112, second paragraph as being indefinite. Claim 52 is considered unclear in describing the structure of the centrifuge tube. This rejection is respectfully traversed.

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While the claim language is difficult, it is clear. The claim is describing use of a centrifuge tube, which has one of three different possible structures, all of which are shown in the Figures. In all configurations, the upper region has the largest internal diameter and the lower region has the least internal diameter. The middle region may be any one of the three possibilities listed in claim 53. It may be of 1) a decreasing diameter from said upper region toward said lower region as shown in Figure 2a for example. The middle region may be 2) a diameter less than said upper region but greater than said lower region as shown in Figure 3e for example. The middle region may be 3) a diameter equal to said lower region, wherein said lower region has a sufficiently small bore to hold an air bubble in it with an aqueous solution above and below it as shown in Figure 9 for example. It is possible for a centrifuge tube to have a configuration that may be interpreted as being more than one of these such as Figure 2b.

Claim 61 was considered vague and indefinite as to the location of the air bubble. The air bubble in claim 61 refers to the air bubble mentioned in claim 53, last two lines. It is the air bubble depicted in the drawings as a round circle. It is entrapped, separating layers of liquid and is temporarily held in place by surface tension. Accordingly, this rejection should be withdrawn.

Claims 52 and 57-60 were rejected under 35 USC 102(e) as being anticipated by Vlasselaer. The examiner contends that Vlasselaer teaches a centrifuge tube with a narrower middle region and a density gradient for separating particles in a liquid. This rejection is respectfully traversed.

While the constriction 12 in Vlasselaer provides a smaller internal diameter and apparently interpreted as a "middle portion", both upper portion 28 and the lower portion 26 have the same diameter as particularly shown in Figures 1a, 1b, 1c and suggested in Figures 2-5 and 7 of Vlasselaer. Present claim 52 recites, "wherein an inner diameter of said upper region is larger than an inner diameter of said lower region". Therefore, Vlasselaer does not anticipate the present claims.

Moreover, Vlasselaer teaches a separation technique for separating one cell type from another cell type. However, there is no concentration of the cells so that one can readily detect that which is not easily detected otherwise. The separation of unwanted cells

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does not result in concentration of the wanted cells because of the excess amounts of liquid gradient material added. Even when recovered, Vlasselaer resuspends the wanted cells in a diluting liquid resulting in no net concentration. Claim 52 recites "A method for concentrating particles..." and "(b) centrifuging said sample in said tube to concentrate said particles" and the specification discusses concentration as a many fold concentration (thousands to a billion fold).

The rejection also argues that the recitation "region has a sufficiently small bore to hold an air bubble in it with an aqueous solution above and below it" is a functional limitation of the centrifuge tube taught by Vlasselaer. This is not correct. Vlasselaer states in column 7, lines 55 to column 8, line 8

"The bottom surface of the constriction member may also may be similarly, slightly angled (although not shown as such in the figures). In an exemplary embodiment, with a tube having an inner diameter of about 2.8 cm, the diameter of opening 14 formed by constriction member 12 is preferably about 0.5 cm. The size of opening 14 is generally not so small as to prevent heavier components of a sample, layered on top of the density gradient solution, from passing through the opening prior to actual centrifugation. Such a movement of components may occur due to normal gravitational forces. In general, the diameter of opening 14 is dictated by the ability to form an increased surface tension across the opening and thereby form an airlock that separates the upper and lower compartments. A restriction that is little more than a rim around the interior of the barrel may be sufficient to provide such a surface tension. Hence, the cross-sectional area of the aperture formed by the constriction member may be as little as about 5% or as great as about 95% of the horizontal cross-sectional surface area of the tube."

An opening of "preferably about 0.5 cm" is considerably larger than that defined in the claims as holding an air bubble. Furthermore, Vlasselaer states, "the aperture formed by the constriction member may be as little as about 5% or as great as about 95% of the horizontal cross sectional surface area of the tube." This is radically different from the present invention where the exemplified centrifuge tube in the present specification has a cross sectional surface area of about 10,000 times less. Note that the present specification states that the centrifuge tube may have differential cross sectional surface area a few orders of magnitude less than even the 10,000 fold difference.

Contrary to the rejection, this is a structural difference and it results in a functional difference to the claimed method. Accordingly, this rejection should be withdrawn.

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New claims 62 and 63 represent further differences from the teachings of Vlasselaer as the particles are pelleted in Vlasselaer rather than banded in liquid. Also, there is no physical barrier between the different fluids in Vlasselaer.

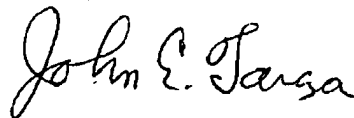
Claims 58 were rejected under 35 USC 103 as unpatentable over Vlasselaer in view of Mason et al. Vlasselaer is applied as above. Mason et al is cited to show purifying viruses by centrifugation. From this the examiner concludes it obvious to use the Vlasselaer method for purifying viruses also. This rejection is respectfully traversed.

Mason et al does not compensate for the basic deficiencies of Vlasselaer as stated above. Mason et al use conventional cylindrical centrifuge tubes. Accordingly, for the reasons given above, this rejection should also be withdrawn.

In view of the above amendments and comments, the claims are now in condition for allowance and applicants request a timely Notice of Allowance be issued in this application. If needed, applicants petition for sufficient extension of time for consideration of this paper.

The commissioner hereby is authorized to charge payment of any fees, including extension of time fees, under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,



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